BEST AVAILABLE IMAGES

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images may include (but are not limited to):

- BLACK BORDERS
- TEXT CUT OFF AT TOP, BOTTOM OR SIDES
- FADED TEXT
- ILLEGIBLE TEXT
- SKEWED/SLANTED IMAGES
- COLORED PHOTOS
- BLACK OR VERY BLACK AND WHITE DARK PHOTOS
- GRAY SCALE DOCUMENTS

IMAGES ARE BEST AVAILABLE COPY.

As rescanning documents *will not* correct images, please do not report the images to the Image Problem Mailbox.

PCT WORLD INTELLECTUAL PROPERTY ORGANIZATION
International Bureau

INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

(51) International Patent Classification 5 : B05B 7/14, 7/24, 9/08

A1

(11) International Publication Number: WO 92/12799

(43) International Publication Date: 6 August 1992 (06.08.92)

(21) International Application Number: PCT/GB92/00087

(22) International Filing Date: 16 January 1992 (16.01.92)

(30) Priority data:
9100950.6 16 January 1991 (16.01.91) GB

(71) Applicant *(for all designated States except US)*: DMW (TECHNOLOGY) LIMITED [GB/GB]; 14 Wilford Bridge Spur, Melton, Woodbridge, Suffolk IP12 1RJ (GB).

(72) Inventor; and

(75) Inventor/Applicant *(for US only)* : DUNNE, Stephen, Terence [GB/GB]; 13 Sawyers, Elmsett, Ipswich, Suffolk IP7 6QH (GB).

(74) Agent: DUMMETT, Thomas, Ian, Peter; Dummett Copp & Co., 14 The Square, Martlesham Heath, Ipswich, Suffolk IP5 7SL (GB).

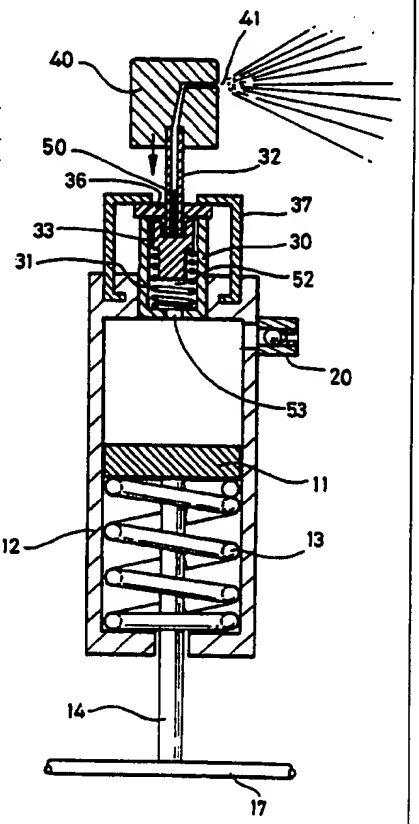
(81) Designated States: AT, AT (European patent), AU, BB, BE (European patent), BF (OAPI patent), BG, BJ (OAPI patent), BR, CA, CF (OAPI patent), CG (OAPI patent), CH, CH (European patent), CI (OAPI patent), CM (OAPI patent), CS, DE, DE (European patent), DK, DK (European patent), ES, ES (European patent), FI, FR (European patent), GA (OAPI patent), GB, GB (European patent), GN (OAPI patent), GR (European patent), HU, IT (European patent), JP, KP, KR, LK, LU, LU (European patent), MC (European patent), MG, ML (OAPI patent), MN, MR (OAPI patent), MW, NL, NL (European patent), NO, PL, RO, RU, SD, SE, SE (European patent), SN (OAPI patent), TD (OAPI patent), TG (OAPI patent), US.

Published
With international search report.

(54) Title: METERED DOSE ATOMISING AND DELIVERY DEVICE

(57) Abstract

The present invention provides a method for forming a flow of fluid into a spray of fine particle size, notably one with a mass median particle size less than 12 micrometres, which method is characterised in that the flow is caused to adopt an annular flow through a duct and in that the velocity gradient within that flow is sufficient to cause shear between components of the flow to break the flow up into a spray, preferably without the need to use a fine nozzle aperture to atomise the flow.



FOR THE PURPOSES OF INFORMATION ONLY

Codes used to identify States party to the PCT on the front pages of pamphlets publishing international applications under the PCT.

AT	Austria	FI	Finland	ML	Mali
AU	Australia	FR	France	MN	Mongolia
BB	Barbados	GA	Gabon	MR	Mauritania
BE	Belgium	GB	United Kingdom	MW	Malawi
BF	Burkina Faso	GN	Guinea	NL	Netherlands
BG	Bulgaria	GR	Greece	NO	Norway
BJ	Benin	HU	Hungary	PL	Poland
BR	Brazil	IE	Ireland	RO	Romania
CA	Canada	IT	Italy	RU	Russian Federation
CF	Central African Republic	JP	Japan	SD	Sudan
CG	Congo	KP	Democratic People's Republic of Korea	SE	Sweden
CH	Switzerland			SN	Senegal
CI	Côte d'Ivoire	KR	Republic of Korea	SU	Soviet Union
CM	Cameroon	LI	Liechtenstein	TD	Chad
CS	Czechoslovakia	LK	Sri Lanka	TG	Togo
DE	Germany	LU	Luxembourg	US	United States of America
DK	Denmark	MC	Monaco		
ES	Spain	MG	Madagascar		

TITLE: METERED DOSE ATOMISING AND DELIVERY DEVICE

The present invention relates to a metered dose atomising and delivery device, notably one in which a dose of medicament is atomised by the velocity gradient within a flow of fluid having an annular flow.

BACKGROUND TO THE INVENTION:

Many forms of device exist for dispensing powders or fluids as sprays. Many of those devices utilise a pressurised propellant to discharge the powder or fluid through a spray nozzle aperture. However, the use of CFC and liquefied gas propellants is becoming increasingly unacceptable from environmental aspects and alternative methods for forming powder or liquid sprays are being saught. This is particularly important where the fluid is a medicament where the medicament is not readily soluble in the propellants used hitherto and the use of co-solvents may introduce secondary components into the medicament composition which are undesirable.

It has been proposed to subject a fluid to a sudden increase in pressure which has been generated mechanically and to eject the pressurised fluid through a very small nozzle aperture to form a spray. However, this requires that the fluid be substantially free from solid particles and/or that the fluid be filtered upstream of the nozzle orifice. Problems of nozzle blockage may thus arise and limit the utility of this method for atomising the fluid.

We have now found that the velocity differential within a flow can be used to generate sufficient shear forces within the flow to cause the flow to break up into a fine particle sized spray without the n ed for a very fine nozzle orifice.

By suitable selection of the operating parameters of the spray device, it is possible to achieve sprays with a mass median particle size of less than 12 micrometres, which is the size required for administration of medicamants via inhalation into the lung of a user. Since the need for a fine nozzle orifice to achieve such fine particle sized sprays may be avoided, the present invention reduces the problems of nozzle blockage with the earlier proposal.

SUMMARY OF THE INVENTION:

Accordingly, the present invention provides a method for forming a flow of fluid into a spray of fine particle size, notably one with a mass median particle size less than 12 micrometres, which method is characterised in that the flow is caused to adopt an annular flow through a duct and in that the velocity gradient within that flow is sufficient to cause shear between components of the flow to break the flow up into a spray, preferably without the need to use a fine nozzle aperture to atomise the flow.

The term annular flow as used herein denotes a flow having substantially concentric annular zones flowing parallel to one another, but with the axial flow velocity increasing towards the radially innermost zone. Alternatively, the flow velocity can increase towards the radially outward zone. For convenience, the invention will be described hereinafter in terms of a flow whose velocity increases towards the centre.

The velocity gradient represents the increase in velocity from one zone to the next and will be a positive gradient towards the centre or longitudinal axis of the duct in which the fluid flows. The velocity gradient may increase progressively so that the zones effectively have no sharp

boundary or interface between one another. However, it is within the scope of the present invention for the gradient to increase stepwise, for example at the interface between two phases of the flow, as when a gas flows through a static measured dose of a powder or fluid to entrain the powder or fluid, or when one fluid flows as a faster stream within a sheath of a slower flowing other fluid, the atomisation being due to the shear action of the velocity differential between the gas flow and the static material or the two fluid flows at the interface between them. Typically, the velocity differential between the radially inward and outward components of the flow will be at least 250 to 350 metres per second.

The shear forces due to the velocity differential which are required to form a flow into a spray will depend upon a number of factors: for example the viscosity and surface tension of the fluid; the pressure drop to which the flow is subjected and the hydraulic diameter of the duct through which the fluid flows; and the particle size required in the spray to be produced.

The fluid can be a gas or a liquid and the flow can be substantially homogeneous, as when an aqueous solution of a medicament is passed through a duct; or can be composed of different phases, as when a gas is used to spray a dose of a fluid or powdered medicament. Thus, the viscosity and surface tension of the fluid can vary over very wide ranges. Where a homogeneous fluid is used, it will usually be preferred that this be an aqueous solution so that the viscosity and surface tension of the fluid typically be similar to that of water, eg. within the ranges 0.75 to 10 Cps at 25°C and 30 to 80 dynes per cm at 25°C. Where a multi-phase fluid is used, the fast flowing fluid is preferably a gas, notably a pulse of pressurised air, and

th other phase is provided by a measured dose of a fluid or powdered medicament through which the gas stream is directed.

The optimum flow velocity differential will also depend upon the pressure drop to which the fluid is exposed as it flows through the duct, in that the higher the pressure drop, the larger the hydraulic diameter which can be used to achieve a given droplet size range spray. The term hydraulic diameter is used herein to denote the cross-sectional area of the duct divided by the one quarter of the circumference of the duct. In the case of a circular cross-section duct, the hydraulic diameter will be the same as the actual diameter. The volume of fluid required to be atomised at each operation of the atomising device will also affect the pressure and hydraulic diameter selected.

For example, where it is desired to form a spray of an aqueous solution with a mass median droplet size less than 12 micrometres, we prefer to operate the method of the invention with an hydraulic diameter in the range 1 to 1000, eg. 5 to 100, micrometres at a pressure differential of from 150 to 500 bar, preferably 200 to 400 bar. However, where a non-homogeneous flow is used so that an interface is formed at which the shear forces act, the pressure differential required to atomise the outer layer of the flow may be as low as from 5 to 50 bar, for example from 6 to 15 bar in the case of a powder which is atomised by a gas flow, and the hydraulic diameter of the duct may be from 500 to 2000, preferably from 500 to 1000, micrometres. The optimum pressure drop and hydraulic diameter can readily be determined in any given case by simple trial and error tests.

Specifically, in th case where an air str am is used to

atomise a dose of a fluid or powd r, we have found that satisfactory atomisation can be achieved with a surprisingly smaller amount of the gas flow than with a conventional nebuliser or other means and with a low pressure drop. Typically, the volume of the gas stream required is less than 5%, typically about 1 to 2% of that required in a nebuliser, thus enabling the method of the invention to be operated in hand portable devices. The volume of the air stream at ambient temperature and pressure is typically from 100 to 1500 times the volume of the fluid or powder to be atomised.

The atomisation of the fluid flow can be achieved in a tubular duct, in which case the spray is usually formed at the open end of the duct as the flow exits the duct. The duct is typically the outlet tube to a pressure generating device, for example pressurised gas container or a spring loaded gas or fluid pump, notably one which is held in the cocked state against the action of a compression spring by a trigger or latch mechanism. The duct can be a smooth walled duct and the length of the duct can be selected over a wide range provided that the length of the duct does not affect the formation of the annular flow by imposing excessive frictional forces at the outer layers of the flow in contact with the duct wall. If desired, the bore of the duct can taper so as to accelerate the flow as it passes along the duct to enhance the atomisation when the flow exits the open end of the duct.

However, it may be preferred to atomise the flow by passing it through a restricted nozzle orifice at the outlet end to a broader diameter duct, the nozzle aperture having a hydraulic diameter in the range specified above and the duct having a greater hydraulic diameter.

The cross-sectional shape of the bore of the duct or of the nozzle aperture is preferably circular, but other cross-section shapes, for example an irregular cross-section or a polygonal cross-section may be used if desired. If desired, several ducts or nozzles may be used to form a more broadcast spray pattern and/or to increase the volume output from a given device, in which case each duct or nozzle aperture preferably has the same hydraulic diameter to provide a substantially even spread of the spray pattern. Where a nozzle aperture is used, it is preferred that any changes in the diameter of the duct or tube feeding the flow of material to the nozzle aperture be decreases in the hydraulic diameter and not increases.

Where the fluid is a liquid, the method of the invention provides a simple method by which the fluid can be atomised into fine droplet sized sprays without the need for a nozzle orifice and thus reduces the cost and complexity of the atomizing devices required and the risk of nozzle orifice blockage. The required dose of such a fluid to be dispensed can be achieved by any suitable means, for example by sucking the required dose into the cylinder of a spring loaded pump which generates the required high pressure and hence flow velocity differentials when the pump mechanism is released and the fluid ejected through a smooth walled duct. Alternatively, the dose of fluid can be achieved by feeding a dose of fluid into an atomisation chamber by injecting the required dose by any suitable mechanism or by a suitable invert and fill dosage mechanism.

Alternatively, notably when a dose of a powder is to be dispensed, the dose can be achieved by mounting a cartridge or other container containing the required amount of fluid or powder upon th outlet to the pump mechanism or other pressurised gas generator, and releasing th pulse of

pressurised air or gas through the cartridge or contain r. Such a cartridge can be formed as a disposable item so that each operation of the pressure generating device requires a new cartridge, thus ensuring accuracy of dosage and minimising the risk of any blockage of the outlet tube which is carrier by the cartridge and hence is replaced with the cartridge.

As indicated above, the fluid or powder to be atomised is preferably a medicament and the invention provides a process for dispensing a medicament which comprises atomising a flow containing the medicament using the method of the invention.

DESCRIPTION OF THE DRAWING:

To aid understanding of the invention, a preferred form thereof will now be described by way of illustration only with respect to the accompanying drawings, in which Figure 1 is a diagrammatic axial cross-section through a device for dispensing a measured dose of a powdered or fluid medicament; and Figure 2 is a diagrammatic axial cross-section through an alternative form of the device of Figure 1.

DESCRIPTION OF THE PREFERRED EMBODIMENT:

A piston 11 is located in a cylinder 12 and loaded by a spring 13. The piston 11 is connected by an axial rod 14 to a handle 17 which allows the piston 11 to be pulled back against the bias of spring 13. As the piston 11 is withdrawn in cylinder 12, it sucks air at ambient pressure into the headspace above the piston 11 in cylinder 12 via port in the wall of the cylinder provided with a non return valve 20. A latch or other det nt mechanism (not shown) acting on handl 17 or rod 14 r tains piston 11 in the fully

retracted position against the bias of spring 13, ie. in the loaded position. When the detent is released, piston 11 moves axially within cylinder 12 to pressurise the air in the cylinder 12 to a pre-determined value dependant on the spring 13 and piston 11 diameter.

An aerosol valve of the conventional female kind is located at the outlet to cylinder 12 and comprises a body 30, a spring 31, a stem 32, a stem holder 33 and a gasket 36. An actuator 40 is mounted above stem 32 and a retaining ring 41 holds said gasket 36 in position.

A predetermined dose of liquid or powdered drug 50 is stored within the stem 32 and this is forced out of the stem and atomised when said actuator 40 is depressed, allowing the pressurised gas in cylinder 12 to flow into passageway 52 via orifice 53. The orifice 53 is sized to control the flow of air into the stem.

When depressed by actuator 40, stem 32 depresses stem holder 33 breaking contact between said holder 33 and seal 36 allowing gas to enter the base of stem 32 and flow through the stored drug 50. By arranging that the volume of air at atmospheric pressure is larger than the volume of liquid drug, substantially annular flow will be set up within stem 32 atomising the liquid as the gas passes up said stem 32 and actuator 40.

In the case where drug 50 is a powder, the annular flow reduces the risk of blockage of the stem bore.

Preferably the ratio of the volume of gas at atmospheric pressure to the volume of liquid drug is greater than 100:1 and preferably between 500:1 and 1500:1. In th case of the powder d drug this ratio can b less than 100:1.

Preferably, the stem 32 with drug 50 and actuator 40 are formed as a detachable unit which can be replaced after each use. In this way, a clean stem and actuator are used for every dose, minimising blockage and contamination. The exit orifice 41 of actuator 40 and the bottom of stem 32 are preferably each sealed with a transverse membrane which is punctured before use.

To help co-ordination of the operation of the device with the breathing in of the user, the actuator 40 could be spring loaded and actuated by a predetermined amount of air flow into lungs set up when the user breathes in. Thus as shown in Figure 2, a body 80 is secured to the cylinder 12 by a snap fit lug 81. A spring 83 is located within said body 80 and exerts a force on the actuator 40 which is prevented from moving by a catch 85, which forms part of a flap 86 hinged at point 87 which when in the ready position blocks off an air passageway 88. A mouthpiece 90 is formed within body 80.

When the patient sucks in through mouthpiece 90, the pressure drops to below atmospheric within body 80 and the difference between atmospheric pressure and the pressure within body 80 causes the flap 86 to move, opening the air passageway 88 to allow air into the mouth through the mouthpiece 90 and releasing catch 85 and allowing spring 83 to push actuator 40 down, activating the device and atomising the drug.

CLAIMS:

1. A method for forming a flow of a fluid into a spray of fine particle size, which method is characterised in that the flow is caused to adopt an annular flow through a duct and in that the velocity gradient within that flow is sufficient to cause shear between components of the flow to break the flow up into a spray.

2. A method as claimed in claim 1, characterised in that the flow is a non-homogeneous flow and the shear occurs at the interface between the phases.

3. A method as claimed in either of claims 1 or 2, characterised in that one phase is a stream of gas and the other phase is a measured dose of a liquid or particulate solid.

4. A method as claimed in claim 1, characterised in that the flow is a substantially homogeneous flow of a liquid.

5. A method as claimed in any one of the preceding claims, characterised in that the velocity differential between the radially inward and external components of the flow is at least 250 metres per second.

6. A method as claimed in any one of claims 1 to 3, characterised in that the pressure differential along the duct is from 5 to 50 bar and the hydraulic diameter of the duct is from 500 to 2000 micrometres.

7. A method as claimed in claim 6, characterised in that the ratio of volume of the gas flow to the volume of the solid or liquid to b atomised is from 100:1 to 1000:1.

8. A method as claimed in claim 4, characterised in that the pressure differential along the flow is from 150 to 500 bar and the hydraulic diameter of the duct is from 5 to 100 micrometres.

9. A method as claimed in any one of the preceding claims, characterised in that the flow is generated by a pressurised gas container or by a pump mechanism which ejects a component of the flow through a tubular duct.

10. A method as claimed in any one of the preceding claims, characterised in that the flow contains a medicament.

11. A method as claimed in claim 10, characterised in that the flow is atomised to a mass median particle size less than 12 micrometres.

12. A method as claimed in any one of the preceding claims, characterised in that the duct is provided with a nozzle aperture outlet having a smaller hydraulic diameter than the hydraulic diameter of the duct.

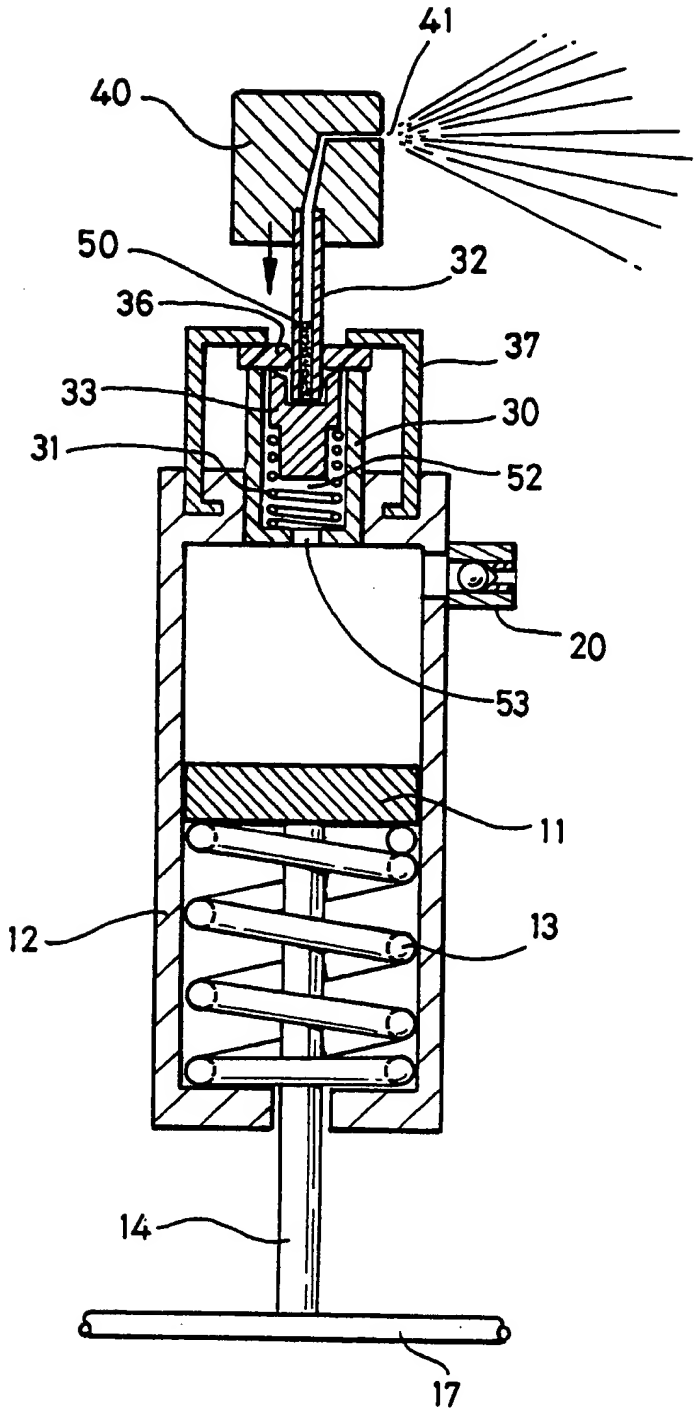


Fig. 1

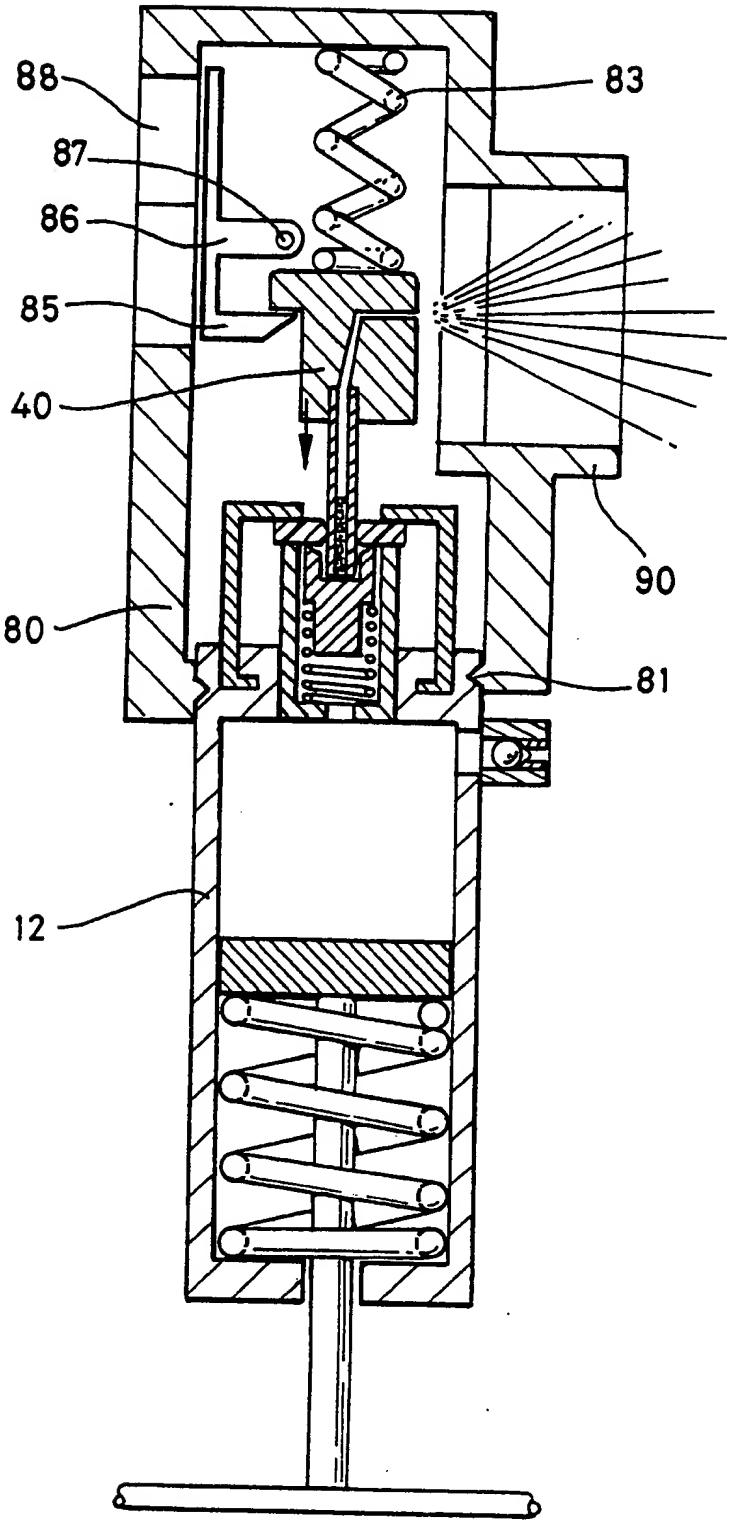


Fig. 2

INTERNATIONAL SEARCH REPORT

International Application No PCT/GB 92/00087

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all)[6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl. 5 B05B7/14; B05B7/24; B05B9/08

II. FIELDS SEARCHED

Minimum Documentation Searched[7]

Classification System	Classification Symbols
Int.Cl. 5	B05B ; A61M

Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in the Fields Searched[8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT[9]

Category[9]	Citation of Document,[11] with indication, where appropriate, of the relevant passages[12]	Relevant to Claim No.[13]
X	FR,A,2 256 084 (CIBA GEIGY AG.) 25 July 1975 see the whole document	1,2,3,9, 10
X	US,A,3 605 744 (DWYER) 20 September 1971 see the whole document	1,4,9,10

[9] Special categories of cited documents :[10]

"A" document defining the general state of the art which is not considered to be of particular relevance

"E" earlier document but published on or after the international filing date

"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)

"O" document referring to an oral disclosure, use, exhibition or other means

"P" document published prior to the international filing date but later than the priority date claimed

"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention

"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
07 APRIL 1992	22.04.92
International Searching Authority	**Signature of Authorized Officer**
EUROPEAN PATENT OFFICE	GINO C.P.G.

ANNEX TO THE INTERNATIONAL SEARCH REPORT ON INTERNATIONAL PATENT APPLICATION NO. GB 9200087 SA 55390

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the European Patent Office EDP file on 07/04/92
The European Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
FR-A-2256084	25-07-75	AU-A- 7671174	24-06-76
		BE-A- 823885	27-06-75
		CA-A- 1011701	07-06-77
		CH-A- 587166	29-04-77
		DE-A- 2461377	10-07-75
		GB-A- 1488719	12-10-77
		JP-A- 50096907	01-08-75
		NL-A- 7416605	30-06-75
		SE-A- 7415243	27-06-75
		US-A- 4017007	12-04-77
US-A-3605744	20-09-71	None	